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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/435,576	11/08/1999	CHIH-MING CHEN	300.1003	5401

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DAVIDSON, DAVIDSON & KAPPEL, LLC
485 SEVENTH AVENUE, 14TH FLOOR
NEW YORK, NY 10018

EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	**PAPER NUMBER**
1616	15

DATE MAILED: 04/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/435,576	Applicant(s) CHEN ET AL.	
	Examiner Sharmila S. Gollamudi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt of the Request for Extension of Time and Request for Reconsideration received on December 23, 2002 is acknowledged. Claims 1-75 are included in the prosecution of this application.

Claim Rejections - 35 USC § 112

Rejection of claims 1-75 under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling is maintained.

Response to Arguments

Applicant argues that the coating is not critical to the instant invention. It is argued that the examiner is limiting the applicant to preferred embodiments. Applicant argues that the specification supports an uncoated formulation with the same release rate.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points to instant specification, page 16 wherein the applicant states that after the coat is formed it coated with "1) an optional protective first coating on the tablet core and/or an optional pH sensitive coating 2) an outer coating comprising a pH sensitive agent and a water insoluble polymer." Secondly, the examiner points to page 18 wherein the applicant describes the mechanism in which the instant invention release the drug: "water is drawn into the tablet and it expands to the point where the outer coating fails in one particular area to form a constricted opening which release the internal contents of the tablet which contain the drug." Clearly the coating provides the controlled release properties of the formulation. Nowhere has applicant provided an

uncoated formulation to support the assertion that the polymer matrix itself can control the instant invention's release properties.

Claims 14, 23-24, 30, 55-56, and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims depend on a parent claim that recites a given range and instant claims are not within the range of the parent claim. For instance claim 1 recites a Tmax of 10-32 hours whereas dependent claim 14 recites a range of 5.3-28.7. Appropriate correction is required.

Claim Rejections - 35 USC § 103

Rejection of claims 1-75 under 35 U.S.C. 103(a) as being unpatentable over Alberts et al (4,997,658) or Cheng et al (Pharmaceutical Research) in view of Oshlack et al (5,472,712).

Alberts teaches a method of lowering plasma cholesterol levels. The method includes administering to a subject a time-controlled drug-delivery device containing an HMG-CoA reductase inhibitor (lovastatin). Alberts discloses that using a sustained or controlled release provides for a single dose to yield an equivalent or improved effect while lowering the peak drug plasma levels (col. 1, lines 39-50). By lowering the amount of plasma concentration in the blood, the potential side effects of the drug are reduced. The controlled release is over a 6 to 24 hour period (col. 2, line 63). Alberts discloses that this controlled release can be achieved by a variety of procedures known to those skilled in the art. The procedures suitable for the invention are diffusion-controlled

systems, osmotic devices, dissolution controlled matrices, and erodible/degradable matrices (col. 3, lines 1-2).

Cheng et al teach the efficacy of a sustained/controlled release dosage form for the delivery of lovastatin or simvastatin. Cheng et al teach lowering cholesterol level. Cheng teaches the lower plasma concentrations of the instant drugs results in equal or better therapeutic efficacy. The instant Cmax is taught (figures).

Alberts or Cheng et al do not specify the formulation for the control release device.

Oshlack et al teach a stabilized control release formulation. The formulation can include various pharmaceuticals, which can provide a therapeutic effect for 12 to 24 hours (col. 4 and col. 5, lines 20). Oshlack provides a once a day administration and teaches Cmax and Tmax of the drug of choice (examples). Oshlack teaches a coating in order to obtain the desired release profiles (Note figures) and manipulation of the release profile by adding release-modifying agents or providing more passageways through the coating (col. 11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Alberts or Cheng and Oshlack since Oshlack provides the guidance for formulating once a day controlled release devices for a therapeutic effect for 12 to 24 hours. One would be motivated to do so since Alberts/Cheng teach the advantages of formulating the instant HMG-CoA inhibitor in a once a day controlled release device. It is further the examiner's position and in the absence of unexpected results that Oshlack provides the general guidance is

formulating a controlled release and depending on the drug, the Cmax will change according to the needed therapeutic dosage; this dosage is taught by Alberts and Cheng.

Response to Arguments

Applicant argues that that the rejection is not directed to the recited functional limitation of the structure. It is argued that Alberts does not teach the use of an aqueous dispersion of ethylcellulose. It is argued that Alberts uses an organic solvent and thus a stability issue is not present; therefore a motivation to combine the references does not exist. Applicant further argues that Oshlack is directed to a wholly different class of therapeutic agents and that Tmax 10-32 hours is not taught.

Firstly, it is requested that applicant note that the motivation has been modified as set discussed in the rejection above; therefore the arguments pertaining to the lack of motivation are moot. However, the examiner does point out that Albert clearly states that any controlled release device is suitable his invention. Secondly in regards to the Tmax, the examiner points to the dependent claims in which the Tmax is within the recited range of Oshlack. It is the examiner's position that Oshlack provides the general guidance to manipulate the release rate and extend Tmax or shorten the time frame by adding release rate modifiers. In figure 16, Oshlack teaches a Tmax of 9 and applicant recites that Tmax is "about" ten hours. It is also noted that standard deviation would have the Tmax fall within the recited range. It is pointed out that Oshlack is relied upon to teach the controlled release formulation and Alberts the primary reference teaches the drug of choice.

Claims 1-75 ar rejected under 35 U.S.C. 103(a) as being unpatentable over Alberts et al (4,997,658) or Cheng et al (Pharmaceutical Research) in view of Sako et al (6,436,441).

Alberts teaches a method of lowering plasma cholesterol levels. The method includes administering to a subject a time-controlled drug-delivery device containing an HMG-CoA reductase inhibitor (lovastatin). Alberts discloses that using a sustained or controlled release provides for a single dose to yield an equivalent or improved effect while lowering the peak drug plasma levels (col. 1, lines 39-50). By lowering the amount of plasma concentration in the blood, the potential side effects of the drug are reduced. The controlled release is over a 6 to 24 hour period (col. 2, line 63). Alberts discloses that this controlled release can be achieved by a variety of procedures known to those skilled in the art. The procedures suitable for the invention are diffusion-controlled systems, osmotic devices, dissolution controlled matrices, and erodible/degradable matrices (col. 3, lines 1-2).

Cheng et al teach the efficacy of a sustained/controlled release dosage form for the delivery of lovastatin or simvastatin. Cheng et al teach lowering cholesterol level. Cheng teaches the lower plasma concentrations of the instant drugs results in equal or better therapeutic efficacy. The instant Cmax is taught (figures).

Alberts or Cheng et al do not specify the formulation for the control release device.

Sako et al teaches a sustained release hydrogel formulation. Sako teaches using polymer weights to manipulate the release rates of the drug (Figures). Further Sako

teaches manipulating the pharmokinectic parameters to yield the desired effect (col. 5 and examples). Lastly, Sako teaches hyperlipemia agents such as pravastatin are suitable for the invention (col. 3, line 4). The reference teaches a once a day formulation for a 24 hour therapeutic release.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Alberts or Cheng and Sako et al since Sako provides the guidance for formulating once a day controlled release devices for a therapeutic effect for 24 hours. One would be motivated to do so since Alberts/Cheng teach the advantages of formulating the instant HMG-CoA inhibitor in a once a day controlled release device. It is further the examiner's position and in the absence of unexpected results that since Sako provides the general guidance for formulating a controlled release, the corresponding values would depend on the drug of choice; these values are taught by Albert and Cheng.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

MICHAEL G. HARTLEY
PRIMARY EXAMINER

SSG

March 28, 2003